Kidney International, Vol. 56, Suppl. 71 (1999), pp. S-238–S-241

Factors associated with calcification of the abdominal aorta in hemodialysis patients

KEIGO KIMURA, YASUSHI SAIKA, HARUHISA OTANI, RYOUICHI FUJII, MASATOSHI MUNE, and SUSUMU YUKAWA

Department of Medicine, Fujii Hospital, Osaka, and Third Department of Internal Medicine, Wakayama Medical College, Wakayama, Japan

Factors associated with calcification of the abdominal aorta in hemodialysis patients.

Background. Cardiovascular and cerebrovascular injury caused by arteriosclerosis has been the major cause of the death in hemodialysis (HD) patients. We quantitatively analyzed and evaluated the severity of abdominal aortic calcification in HD patients in comparison to risk factors for arteriosclerosis.

Methods. One hundred thirty-seven HD patients were examined. Using image analysis software, areas of the calcified abdominal aorta were quantitatively analyzed on plain computerized tomography images. Other factors such as blood pressure (BP), lipid levels, and calcium (Ca) × phosphorus (Pi) value were also analyzed.

Results. Patients with a higher one-year average of systolic BP showed a higher severity of abdominal aortic calcification. That is, the severity of abdominal aortic calcification in patients with a one-year systolic BP average above 160 mm Hg was 31.5 ± 13.6%, and this severity was significantly higher than that in patients with a one-year systolic BP average of less than 120 mm Hg (8.0 ± 7.7%, $P < 0.01$). The severity of abdominal aortic calcification in patients demonstrating risk values of ectopic calcification, that is serum Ca × Pi ≥ 60 (mg/dl), on more than 4 of 24 measurements within one year (25.8 ± 13.6%) was significantly higher than the severity of aortic calcification in patients demonstrating this value less than four times in one year ($P < 0.05$). There was no correlation between levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, lipoprotein(a), and severity of abdominal aortic calcification.

Conclusions. Systolic BP levels and the product of serum Ca and Pi were related to the severity of abdominal aortic calcification in HD patients. These observations suggested that BP control, as well as control of serum Ca and Pi levels, was important in preventing the progression of abdominal aortic arteriosclerosis.

Cardiac and vascular complications such as cardiac failure, myocardial infarction, and cerebrovascular injury caused by arteriosclerosis have been the major causes of death in hemodialysis (HD) patients [1, 2]. This is due to the numerous factors that can accelerate arteriosclerosis in HD patients that do not exist in healthy individuals. We have semiquantitatively evaluated the calcification of the abdominal aorta using an aortic calcification index (ACI) [3] and correlated this index with risk factors for arteriosclerosis in HD patients. This study introduces an alternative method to the ACI to quantitate calcification on simple abdominal computerized tomography scans in order to better clarify arteriosclerotic risk factors in HD patients.

Key words: arteriosclerosis, abdominal aortic calcification, blood pressure, hemodialysis.

METHODS

Subjects

We examined 137 HD patients (70 male and 67 female). This average age was 59.7 ± 11.9 years, and they had been on HD for an average of 80.5 ± 64.5 months. Of the 137 patients, 34 were complicated by diabetes, and they had been on dialysis for an average of 51.7 ± 41.5 months.

Lipid analysis

Levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), and lipoprotein(a) [Lp(a)] were followed for one year to obtain a one-year average. Levels of LDL-C were calculated using Friedewald's equation (LDL-C = TC − HDL-C − TG/5).

Aortic calcification area index measurement

The aortic calcification area index (ACAI) is measured as follows: The area above the bifurcation of the common iliac artery is scanned 10 times at 1 cm intervals. These scans are then analyzed by NIH Image 1.61 to calculate the area of calcification in the abdominal aorta and the cross-sectional area of the aorta. The calcification area in the abdominal aorta is divided by the cross-sectional area of the aorta to calculate the extent of calcification as a percentage. The ACAI is the average calcification of 10 scans.

Blood pressure

Systolic and diastolic blood pressure (BP) was measured an average of 156 times just before starting each HD session during 1996. The average systolic and diastolic BPs over the year were calculated for each patient.

Calcium × phosphorus value

The effect of serum calcium (Ca) × phosphorus (Pi) values on aortic calcification areas was analyzed as follows: The levels of serum Ca and Pi were measured twice a month for a year (total of 24 measurements). Serum Ca × Pi values of greater than 60 were considered as risk factors for ectopic calcification. The number of occasions that serum Ca × Pi was greater than 60 was then tabulated for each patient. The patients were divided into those with less than four episodes of high serum Ca × Pi (favorably controlled group) and those with four or more episodes of high serum Ca × Pi (poorly controlled group).

Statistical analysis

Results were expressed as mean ± SD. Statistical differences between groups were assessed by Student's *t*-test or one-way analysis of variance, depending on the number of comparisons being made. Pairwise multiple comparisons for significant analyses of variance were made by Fisher's protected least significant differences (PLSD) tests. *P* values of less than 0.05 were considered significant.

RESULTS

Age and sex

The ACAI tended to be higher among the older patients. A comparison of the ACAI of men in their 40s (17.7 ± 10.3%, $N = 8$) was significantly higher than that of women in the same age group (4.0 ± 3.7%, $N = 10$, $P < 0.01$), indicating that abdominal aortic calcification develops earlier in men than women.

Dialysis history

Age appears to be strongly related to the degree of calcification of the abdominal aorta. The average age of dialysis patients is approximately 60 years of age. Thus, we examined the relationship between the length of HD and the ACAI in nondiabetic patients between 55 and 64 years of age. The ACAI of patients who had been on dialysis for 60 or more months (25.2 ± 13.2%, $N = 28$) was significantly higher than that of patients who had been on HD for less than 12 months (5.3 ± 5.6%, $N = 4$) or between 12 and 36 months (7.4 ± 6.4%, $N = 5$, $P < 0.01$).

Diabetes

To eliminate the effect of the length of HD on the relationship between diabetes and ACAI, patients between the ages of 55 and 64 years who had been on HD for less than 36 months were analyzed. The ACAI of patients with accompanying diabetes (26.5 ± 15.1%, $N = 7$) was significantly higher than that of nondiabetic patients (6.5 ± 5.8%, $N = 9$, $P < 0.01$).

Lipid

There were no apparent correlations between levels of LDL-C, HDL-C, TG, Lp(a), and the ACAI.

Blood pressure

The relationship between systolic BP and ACAI was investigated in nondiabetic patients between the ages of 55 and 64 years. A higher average systolic BP measure over the course of one year tended to be associated with a higher ACAI. The ACAI of patients with an average systolic BP above 160 mm Hg (30.2 ± 12.9%, $N = 6$, $P < 0.01$) or patients with an average systolic BP equal to or higher than 140 but less than 160 mm Hg (22.4 ± 14.4%, $N = 14$, $P < 0.05$) was significantly higher than that of patients with an average systolic BP of less than 120 mm Hg (8.0 ± 7.7%, $N = 5$; Fig. 1A). There was no significant relationship between diastolic BP and ACAI (Fig. 1B).

Calcium × phosphorus value

The relationship between a serum Ca × Pi value of greater than 60 (mg/dl) and the ACAI was investigated in patients between 55 and 64 years of age. The ACAI of patients with poorly controlled levels of Ca and Pi who had four or more high serum Ca × Pi levels (≥60) out of 24 tests in a one-year period (26.1 ± 13.0%, $N = 35$) was higher than that of patients with well-controlled levels of Ca and Pi who had fewer than four high serum Ca × Pi results (17.8 ± 17.2%, $N = 20$, $P < 0.05$; Fig. 2A). The relationship between serum Ca × Pi values and ACAI with respect to diabetes was investigated. The ACAI was significantly higher among diabetic patients with poorly controlled Ca and Pi levels (35.3 ± 12.1%, $N = 10$) than that of well-controlled Ca and Pi levels (14.9 ± 16.4%, $N = 7$, $P < 0.01$; Fig. 2B). There were no apparent correlations between parathyroid hormone level and ACAI (data not shown).

DISCUSSION

Cardiac and vascular complications caused by arteriosclerosis such as cardiac failure, myocardial infarction, and cerebrovascular accidents are the major causes of death among HD patients. This appears related to the greater number of risk factors in HD patients. HD patients often present with hypertension before the start of HD, and once HD begins, arteriosclerosis may progress at a faster rate in these patients because of multiple

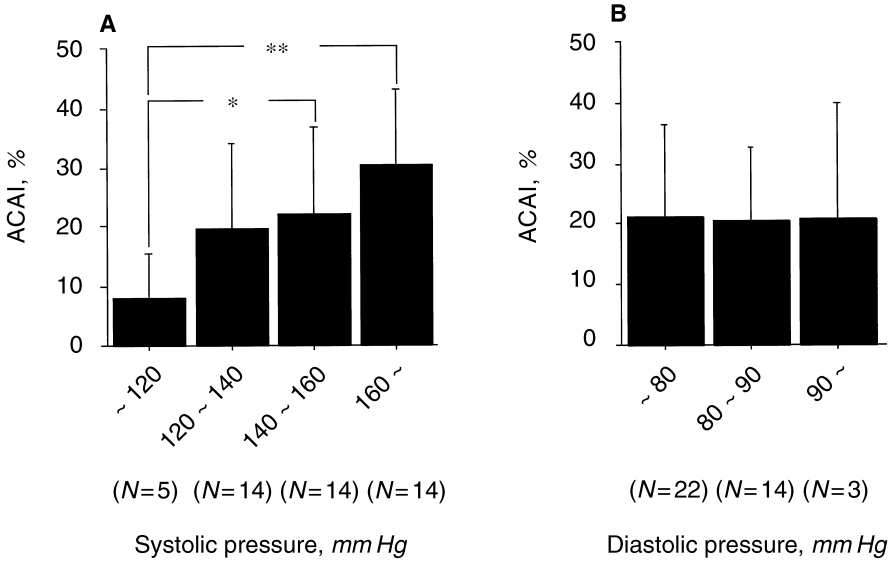

Fig. 1. Influence of blood pressure on aortic calcification area index (ACAI). (*A*) The relationship between systolic pressure and ACAI was investigated in nondiabetic patients between the ages of 55 and 64 years. The data are presented as mean ± SD. $*P < 0.05$; $**P < 0.01$. (*B*) The relationship between diastolic pressure and ACAI was investigated in nondiabetic patients between the ages of 55 and 64 years. The data are presented as mean ± SD.

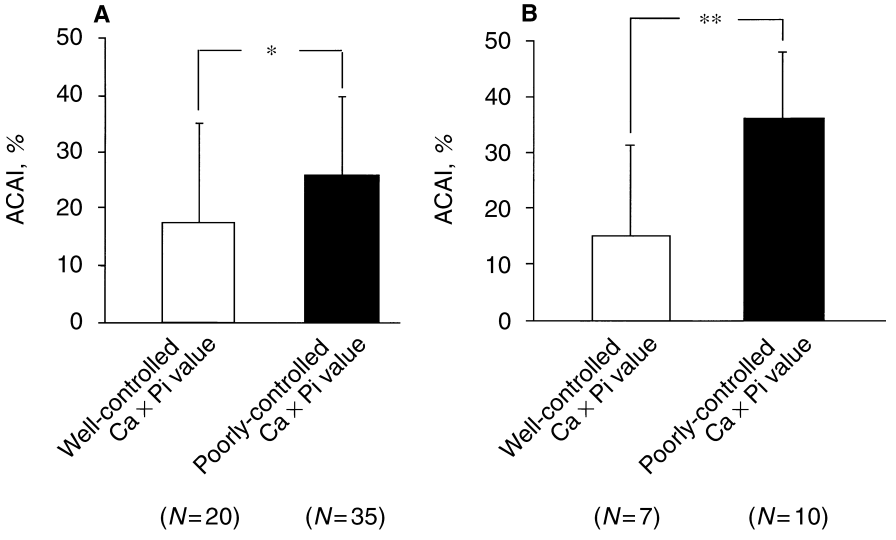

Fig. 2. Comparison of aortic calcification area index (ACAI) between well-controlled group and poorly controlled group in the serum Ca × Pi product. (*A*) The relationship between serum Ca × Pi values and ACAI was investigated in all patients between 55 and 64 years of age. The data are presented as mean ± SD. $*P < 0.05$. (*B*) The relationship between serum Ca × Pi values and ACAI was investigated in diabetic patients between 55 and 64 years of age. The data are presented as mean ± SD. $**P < 0.01$.

metabolic disorders including Ca, Pi, and lipids. Degoulet et al suggested a significant relationship between elevated systolic and diastolic BP and the mortality rate from cardiovascular diseases [4]. The severity of arteriosclerosis is particularly high among diabetic dialysis patients than those who are treated with HD for other causes. In addition to aging, increased serum Ca × Pi [5] and secondary hyperparathyroidism [6] have been suggested as progression factors for abdominal aortic calcification in HD patients. Despite evidence that Ca and Pi metabolism plays a role in abdominal aortic calcification, a clear relationship between abdominal aortic calcification and yearly average serum Ca × Pi levels has not been established. In this study, we divided the subjects into those who frequently had a high serum Ca × Pi value (four or more times out of the 24 tests a year) and those who had a low frequency of an elevated serum Ca × Pi value (less than four times a year). In this way, we were able to demonstrate the effect of Ca and Pi on abdominal aortic calcification. In conclusion, systolic BP and serum Ca × Pi values correlated with calcification of the abdominal aorta in HD patients, suggesting that control of BP and Ca and Pi metabolism is essential in preventing the progression of abdominal aortic arteriosclerosis.

Reprint requests to Haruhisa Otani, M.D., Third Department of Internal Medicine, Wakayama Medical College, 811-Kimiidera, Wakayama, 641-0012, Japan.
E-mail: hotani@wakayama-med.ac.jp

REFERENCES

1. Lindner A, Charra B, Sherrard DJ, Scribner BH: Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 290:697–701, 1974
2. Statistical Committee: An overview of regular dialysis treatment in Japan as of Dec. 31, 1997. *Annual Report of Japanese Society for Dialysis Therapy*, 1998
3. Yukawa S, Sonobe M, Tone Y, Yukawa A, Mimura K, Mune M, Maeda T, Nomoto H, Nishide I: Prevention of aortic calcification in patients on hemodialysis by long-term administration of vitamin E. *J Nutr Sci Vitam* 38(Suppl):S187–S190, 1992
4. Degoulet P, Legrain M, Reach J, Aime F, Devries C, Rojas P, Jacobs C: Mortality risk factors in patients treated by chronic hemodialysis: Reports of the diaphane collaborative study. *Nephron* 31:103–110, 1982
5. Milliner DS, Zinsmeister AR, Lieberman E, Landing B: Soft tissue calcification in pediatric patients with end-stage renal disease. *Kidney Int* 55:289–315, 1990
6. De Francisco AM, Ellis HA, Owen JP, Cassidy MJD, Farndon JR, Ward MK, Kerr DSN: Parathyroidectomy in chronic renal failure. *Q J Med* 55:289–315, 1985